REMARKS

By the amendments presented, the specification has been amended to correct typographical errors at page 6, lines 3-4 in recitation of commas rather than colon, and in reciting the singular terms "analgesic" and "antipyretic" rather than the plural terms "analgesics" and "antipyretics".

Also by the amendments presented, Claim 21 has been amended to correct a typographical error in recitation of the term "analygesic mucolytics" rather than the terms "analgesics" and "mucoltyics".

Also by the amendments presented, Claim 26 has been amended to delete reference to the claimed pharmaceutical active component having a molecular weight of less than 500 grams per mole, and this molecular weight claim limitation has been incorporated into Claim 21.

Also by the amendments presented, Claim 28 has been amended to depend from Claim 21 rather than from canceled Claim 27.

Attached hereto is a marked-up version of the changes made to the specification and claims as a result of the current amendments. The attached page is captioned **"Version with Markings to Show Changes Made"**.

Upon entry of the amendments presented, Claims 21-26 and 28-36 remain in this continuation examination application. No additional claims fee is due.

Invention Synopsis

The present invention is directed to stable liquid compositions which comprise a select pharmaceutical active and a reducing agent, wherein the reducing agent provides for improved stability of these compositions especially when the compositions are formulated into various product forms such as liquid elixirs for treating symptoms associated with respiratory illnesses.

It has been found that a reducing agent can be included in liquid compositions containing a select pharmaceutical active to enhance long term stability of the composition, provided that the reducing agent is solubilized in a solvent system separately from a solvent system used to solubilize the active. The solubilzation of the reducing agent in one solvent phase, and the active in another solvent phase, results in a stable, homogenous, liquid composition that is highly effective in the delivery of select pharmaceutical active ingredients.

Formal Matters

a) Specification

The specification has been objected to for typographical errors at page 6, lines 3-4, in reciting "commas" rather than "colons" after the described active components. Responsive to this objection, the specification has been amended to correct the typographical errors, thus obviating this objection.

b) Claims

Claims 21-26 and 28-36 have been rejected under 35 U.S.C. 112 (2nd paragraph) as being indefinite for reciting in Claim 21 the term "analgesic mucolytics". Responsiv t this rejection, Claim 21 has been amended to recite the terms "analgesics" and "mucolytics" rather than the term "analgesic mucolytics", thus obviating this rejection as it would apply to amended Claim 21. Applicants submit that this rejection is also obviated as it applies to Claims 22-26 and 28-36 which either depend or refer to amended Claim 21.

Art Rejections

a) Rejection under 35 U.S.C. 102 over Riess et al.

Claims 21-23, 26, 28, 29, 32, 34, and presumably 31 have been rejected under 35 U.S.C. 102 as being anticipated by Riess et al. (U.S. Patent 5,190,947). The Examiner contends that Riess et al. disclose an oral pharmaceutical composition as taught by Applicants, wherein the oral pharmaceutical composition comprises an analgesic drug, sodium metabisulfite, and solvents including propylene glycols. Applicants respectfully traverse this rejection as it would apply to the amended claims.

Riess et al. disclose oral pharmaceutical compositions which comprise an analgesically effective amount of a codeine salt of [2-[(2,6-dichlorophenyl)-amino]-phenyl]-acetic acid (i.e., diclofenac-codeine salt). Riess et al. further disclose that the oral pharmaceutical compositions include unit dose forms of tablets, enteric-coated tablets, dragées, and capsules, and that to prepare tablets and dragée cores the diclofenac-codeine salt is combined with ingredients such as polyethylene glycols. The oral capsules are described as dry-filled capsules and soft, sealed capsules, wherein the soft sealed capsules comprise the diclofenac and codeine active ingredients dissolved or suspended in polyethylene glycols, and optionally stabilizers such as sodium metabisulfite or ascorbic acid. Riess et al., however, fail to disclose an oral pharmaceutical composition which comprises a pharmaceutical active selected from analgesics, wherein the pharmaceutical active has a molecular weight of less than 500 grams per mole.

Applicants submit that the Riess et al. reference fails to anticipate Applicants' Claims 21-23, 26, 28, 29, 31, 32, 34, as amended, wherein these amended claims are now limited to an oral composition which comprises a select pharmaceutical active having a molecular weight of less than 500 grams per mole. Riess et al. teach oral pharmaceutical compositions comprising an analgesic pharmaceutical active that is a codeine salt of [2-[(2,6-dichlorophenyl)-amino]-phenyl]-acetic acid dissolved in polyethylene glycols, and a sodium metabisulfite stabilizer. By contrast, Applicants' Claims 21-23, 26, 28, 29, 31, 32, 34, as amended, are limited to an oral composition which comprises a select pharmaceutical active having a molecular weight of less than 500 grams per mole, a solvent including polyethylene glycol, and a reducing agent including sodium metabisulfite.

Applicants submit that a codein salt of [2-[(2,6-dichlorophenyl)-amino]-phenyl]-acetic acid as taught by Riess et al. has a molecular weight of 595.5 grams per mol . By contrast, Applicants Claims 21-23, 26, 28, 29, 31, 32, 34, as amended, are limited to a pharmaceutical active including analgesics that has a molecular weight of less than 500 grams per mole. Accordingly, the Ricss et al. reference fails to teach the molecular weight limitation of Applicants' claimed pharmaceutical active component.

In view of the foregoing remarks, Applicants submit that the Riess et al. reference fails to teach each and every limitation of Applicants' Claims 21-23, 26, 28, 29, 31, 32, and 34, as amended. Rejection of these claims as being anticipated by Riess et al. is improper and, therefore, should be withdrawn.

b) Rejection under 35 U.S.C. 103 over Riess et al.

Claims 21-26 and 28-36 have been rejected under 35 U.S.C. 103 as being unpatentably obvious over Riess et al. (U.S. Patent 5,190,947). The Examiner contends that Riess et al. disclose compositional ingredients as claimed by Applicants, and that it would have been obvious to optimize the concentration ranges of these ingredients as well as provide a method for treating respiratory illnesses using Riess et al.'s composition, to thereby realize Applicants' invention.

Riess et al. disclose oral pharmaceutical compositions which are suitable for administration in the alleviation of pain, and which comprise an analgesically effective amount of a codeine salt of [2-[(2,6-dichlorophenyl)-amino]-phenyl]-acetic acid (i.e., diclofenac-codeine salt). Riess et al. further disclose that the oral pharmaceutical compositions include unit dose forms of tablets, enteric-coated tablets, dragées, and capsules, and that to prepare tablets and dragée cores the diclofenac-codeine salt is combined with ingredients such as polyethylene glycols. The oral capsules are described as dry-filled capsules and soft, sealed capsules, wherein the soft sealed capsules comprise the diclofenac and codeinc active ingredients dissolved or suspended in polyethylene glycols, and optionally stabilizers such as sodium metabisulfite or ascorbic acid. Riess et al., however, fail to disclose an oral pharmaceutical composition which comprises a pharmaceutical active selected from analgesics, wherein the pharmaceutical active has a molecular weight of less than 500 grams per mole.

Applicants submit that the Riess et al. reference fails to teach or suggest the oral composition of Applicants' amended Claims 21-26 and 28-36, wherein these amended claims are directed to an oral composition which comprises a select pharmaceutical active having a molecular weight of less than 500 grams per mole. Riess et al. teach and suggest oral pharmaceutical compositions which comprise a diclofenac-codiene salt analgesic active that has a molecular weight of 595.5 grams per mole. By contrast, Applicants' amended Claims 21-26 and 28-36 are now limited to a pharmaceutical active including analgesics that has a molecular weight of less than 500 grams per mole.

The Examiner contends that, in view of the teachings and sugg stions of Riess et al., it would have been obvious to realize Applicants' invention of Claims 21-26 and 28-36 because the Riess et al. referenc teaches and suggests the pharmaceutical active, solvent, and reducing agent elements of these claims, and that those features of Applicants' Claims 21-26 and 28-36 that are not taught or suggested by Riess et al. are known features within the gambit of the skilled artisan. First, Applicants submit that the Riess et al. reference fails to teach or suggest the pharmaceutical active's molecular weight limitation of Applicants' Claims 21-26 and 28-36, as amended. Secondly, known knowledge combined with the teachings and suggestions of Riess et al. would still not result in an oral composition comprising Applicants' now claimed pharmaceutical active component.

Riess et al. teach and suggest oral pharmaceutical compositions which comprise an analgesic pharmaceutical active that has a molecular weight outside the range of Applicants' claimed pharmaceutical active, and this particularly applied reference, as suggested by the Examiner, may provide motivation to formulate an oral pharmaceutical composition comprising a diclofenac-codiene salt pharmaceutical active, a polyethylene glycol solvent, and a sodium metabisulfite stabiliser, but not Applicants' now claimed oral composition of Claims 21-26 and 28-36 which comprises a select pharmaceutical active including analgesics that have a molecular weight of less than 500 grams per mole, a solvent including polyethylene glycol, and a reducing agent including sodium metabisulfite. The Riess et al. reference fails to teach or suggest Applicants' now claimed oral composition.

In view of the foregoing remarks, it is submitted that the Riess et al. reference fails to teach or suggest the oral composition of Applicants' Claims 21-26 and 28-36, as amended. Accordingly, rejection of these claims as being unpatentably obvious over Riess et al. is improper, and should be withdrawn.

Conclusions

Applicants have made an earnest effort to place their application in proper form and to distinguish the claimed invention from the applied prior art. WHEREFORE, reconsideration of the application, withdrawal of the rejections under 35 U.S.C. 112 (2nd paragraph) and 35 U.S.C. 102 and 103, and allowance of Claims 21-26 and 28-36 are respectfully requested.

Respectfully submitted,
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V rsion with Markings to Show Changes Made

IN THE SPECIFICATION:

The specification has been amended as follows:

At page 6, lines 1-10, the paragraph has been amended as follows:

--The actives that comprise compositions of the present invention include actives that fall into at least one of the following pharmacological classifications: antitussives; antihistamines; non-sedating antihistamines; decongestants; expectorants; mucolytics[,]; [analgesic,] analgesics; antipyretics; anti-inflammatory agents[,]; local anesthetics; and mixtures thereof. References that describe the use of such actives include J. G. Hardman, The Pharmacologic Basis of Therapeutics, Ninth Edition, McGraw-Hill, New York, 1995. Among the actives that fall in these pharmacological classifications are those that are suited for absorption through mucosal tissues. These actives can be used alone or in combination with other actives not necessarily absorbed in this manner and may be formulated within existing formulation techniques.--

IN THE CLAIMS:

Claims 21, 26, and 28 have been amended as follows:

Claim 21. (3rd Amendment) An oral composition comprising:

(a) a pharmaceutical active selected from the group consisting of antitussives, antihistamines, non-sedating antihistamines, decongestants, expectorants, analgesics, mucolytics, antipyretics, anti-inflammatory agents, local anesthetics, and mixtures thereof;

(b) a hydrophilic, water-miscible, anhydrous solvent wherein the pharmaceutical active in its un-ionized form has a percent solubility value in the solvent at ambient temperature that is equal to or greater than 0.075% and the pharmaceutical active is in its free, un-ionized form as a monomolecular dispersion in the solvent; and

(c) a reducing agent wherein the reducing agent has an E^0 value equal to or greater than about -0.119V.

Claim 26. (Amended) The composition according to claim 21 wherein the pharmaceutical active [has a molecular weight of less than 500 grams per mole,] is capable of being ionized when the composition comprises an aqueous solvent, and in its un-ionized form has an octanol-water partition coefficient of at least 100.

Claim 28. (Amended) The composition according to claim [27] 21 wherein the pharmaceutical active is in the solvent at a concentration of less than or equal to 125% of the percent solubility value of said active.